UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,345	09/16/2003	Levon Arakelyan	Q71975	2068

23373 7590 04/19/2007

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
CLOW, LORI A	
ART UNIT	**PAPER NUMBER**
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/662,345	ARAKELYAN ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *10 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11 and 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 February 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 31 January 2007, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-17 are currently pending. Claims 10 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 20 April 2006. Claims 1-9, 11, and 13-17 are examined herein.

Drawings

The replacement drawings submitted 2 February 2007 are accepted.

Specification/Abstract

This objection is re-iterated from the previous Office Action. Applicant has not addressed this issue in the response.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range **of 50 to 150 words**. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means"

and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 11, and 13-17 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for some of the reasons set forth in the previous Office Action. The pertinent rejections are re-iterated below. Those rejections that are not re-iterated have been withdrawn in view of the amendments to the claims.

1. Claim 1, step (b) recites "performing a phase I clinical research in which a clinical trial on at least a single dose is performed in parallel with performing computer simulation studies using the computer model". It is unclear what using the model is simulating? Is the model simulating the clinical research? Clarification is requested.

Applicant argues that the model is the model of the disease in question along with the given drug model. This model describes the evolution of the disease along time and the way it is affected along time by the administration of a certain amount of a given drug. Again, the model constitutes equations for computing the effects of the drug on the disease, where computer

programs do the actual computation. The execution of these computer programs is referred to as computer simulations, as it simulates on the computer the real life disease process and the way the disease and organism is affected by a given treatment.

This is not persuasive. The claim is still unclear. Is it the computer model that interacts with the simulation studies or are the two just run in parallel with no connection to one another? Is simulation performed on the data from patients, for instance? Clarification is requested.

2. Claim 1, step (c) recites "adjusting the computer model based upon comparison of the results of the clinical research and the computer simulation". What about the computer simulation is being compared to the clinical research? Are the similarities, differences, or both being compared, for example? Clarification is requested.

Applicant argues that the outcomes of the computer simulation, that is, the prediction of the effects of a certain drug protocol on a disease process (i.e., tumor size in certain time points), is compared to results of a real life clinical trial in which a real patient with the same disease is administered the same drug using the same protocol. All real lie effects of the drug on the disease are being compared, both similarities and differences. In cases there are differences, the model is adjusted by changing the equations to minimize the differences as much as possible.

This is not persuasive. The claim remains unclear. No "real life clinical trial" is claimed such that the comparison step in the claim is clear. Further, no equations are clear such that it is clear that the model can be adjusted.

3. Claim 1, step (e) recites "checking the drug for cumulative effects and providing this information to the computer model". It is unclear as to what cumulative effects are being "checked". Clarification is requested.

Applicant argues that cumulative effects are the effects of drug on both disease and organism after it was administered more than once, taking into account the previously administered amounts.

This is not persuasive, as cumulative effects after administration have not been claimed. Thus the claim remains indefinite as to what cumulative effects are checked.

4. Claim 1, step (h) recites "performing phase II clinical trial where a number of small scale clinical trials are performed in parallel based upon the results of step g. It is unclear as to what results the claim refers? What results in step g are being used? Clarification is requested.

Applicant argues that step (g) provides different optimal treatment protocols predictions for different pairs of a clinical indication and a patient population. For each prediction of an optimal treatment protocol, a phase II clinical trial is performed applying the optimal treatment protocol to patients belonging to the appropriate patient subpopulation having the appropriate clinical indication.

This is not persuasive, as step (h) does not include any limitations with regard to providing protocol predictions for different pairs of clinical indications and patient populations. Therefore, the claim remains unclear as to what results of step (g) are implemented for small-scale clinical trials.

5. Claim 2 recites "wherein step b, prior to each sub-step of the phase I trial". There is insufficient antecedent basis in the claim for "each sub-step", as no sub-step is recited in step (b). Clarification is requested.

Applicant argues that indeed the sub-step is not a sub-step of claim 1 step (b), but as clearly indicated in the claim a sub-step of Phase I clinical trial.

This is not persuasive. Claim 1, step (b) does not recite a sub-step of the Phase I trial. Claim 1, step (b) does not even recite a Phase I trial. Rather, it recites a phase I clinical research and a clinical trial, but not a Phase I trial. The claim continues to lack antecedent basis.

6. Claim 2 recites, "the computer model is adjusted based upon the comparison". It is unclear as to what about the comparison is used to adjust the computer model. Clarification is requested.

Applicant argues that as explained in issue 1 above, regarding the comparison, which requires model adjustment. The researcher compares the results of the real life studies to the predictions of the model. In case these prediction turn out to be not as accurate as required, the model should be changed/adjusted so that it gives more accurate results. The models are adjusted by changing the equations to result different outcomes to the same calculations.

This is not persuasive. As stated above, no "real life clinical study" is claimed such that the comparison step in the claim is clear. Further, no equations are claimed such that it is clear that the model can be adjusted.

7. Claim 9 recites "a second decision". This is unclear, as no first decision was determined. Clarification is requested.

Applicant argues that first decision was mentioned in Claim 3 and as explained above referred to the decision whether to continue Phase II clinical trials. The second decision refers to the decision whether to continue to the Phase III clinical trial.

This is not persuasive. Applicant will note that claim 9 depends from claim 8. Claim 8 depends from claim 1 and not from claim 3. Therefore, there remains a lack of antecedent basis in the claim for a "second decision".

The rejections above under 112, 2nd paragraph are maintained.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 11, and 13-17 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of performing interactive clinical trials for testing a new drug for cancer related studies, does not reasonably provide enablement for method of performing interactive clinical trials for testing a new drug for any know n disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use or make the invention commensurate in scope with these claims. The rejection is re-iterated below.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to perform the interactive clinical trials for testing a new drug for any known disease. As will be outlined below, this constitutes undue experimentation.

b) and c) The specification provides examples for performing such a method in the scope of cancer related studies. For example, the specification discloses, at paragraph [52] that "these include the data of experiments using different tumor types". At paragraph [53] the specification teaches that "this again includes data on different tumor types". The specification states at paragraph [67] that "at this point many simulations are carried out on different cancer types in order to find the optimum protocol for different patient populations".

d) The invention is drawn to methods for performing the interactive clinical trials on any disease. However, the specification is enabled only for performing these methods for cancer.

e) and g) It would have been well known in the art that performing computer modeling is specific for various diseases, based upon the databases that are being employed. For instance, efficacy modeling for tumors would follow a different mathematical protocol from that of modeling for another disease, such as diabetes, for example. Iliadis et al. (Computers and Biomedical Research (2000) Vol. 33, pages 211-226; PTO 1449 reference 30). Teach a specific algorithm to assess tumor growth, in which efficacy is measured. The instant specification is drawn to cancer modeling and therefore, cancer modeling is enabled.

f) The skill of those in the art of molecular biology/bioinformatics is high.

h) The claims are broad because they are drawn to a method applicable to any and all diseases. The skilled practitioner would first turn to the instant specification for guidance to practice methods. However, the instant specification is enabled only for cancer related embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that tumor biology and efficacy modeling is specific. Finally, said

practitioner would turn to trial and error experimentation. Such represents undue experimentation.

Response to Arguments

Applicant has provided no arguments with regard to the lack of enablement of the instant, pending claims. Applicant simply states that the Examiner is incorrect and points the Examiner to the steps recited in the 112, 2nd arguments. As there is no correlation between the rejections set forth by the examiner in the enablement rejection and those arguments of Applicant in the 112, 2nd rejection, this line of reasoning is insufficient to overcome the rejection and the Examiner maintains the rejection for the reasons set forth above. Applicant is reminded that the burden falls on the applicant to present persuasive arguments, supported by suitable proofs where necessary, that one skilled in the art would have been able to make and use the claimed invention using the disclosure as a guide. In re Brandstadter, 484 F.2d 1395,179 USPQ 286 (CCPA 1973).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15-17 remain rejected under 35 U.S.C. 102(b) as being anticipated by Iliadis et al. (Computers and Biomedical research (2000) Vol. 33, pages 211-226; PTO 1449 Reference 30).

The rejection is re-iterated below.

The instant claims are drawn to a method for performing clinical trials for a new drug comprising performing pre-clinical phase in which a computer model for pk/pd is created; a method for performing clinical trials for a new drug comprising performing phase I clinical trial wherein dose-escalation trial is performed with computer simulation; and a method of performing clinical trials for a new drug comprising developing a strategy for a next sub-step in phase I in conjunction with computer predictions.

Iliadis et al. teach a method in which optimization of cancer treatment is determined by using a mathematical model of pharmacokinetics of anticancer drugs, antitumor efficacy, and drug toxicity (abstract). The first approach relies on modeling to simulate the fate of drug concentration, tumor size, and WBC count (page 218, paragraph 5) (claim 15). The second phase involves protocol implementation, based upon the model (page 218, paragraph 7) (claim 16). The protocols are used clinically, as outlined on page 219. Lastly, optimization of the protocols is performed (page 219, paragraph 5) (claim 17).

Response to Applicant's Arguments

1. *Applicant argues that claims 15-17 are related to interactive clinical trials. A general teaching that protocols are used clinically as in Iliadis cannot be construed to be a specific disclosure related to interactive clinical trials.*

This is not persuasive. Firstly, the specification fails to specifically define "interactive clinical trial". The specification describes a design in which an "in silico" patient engine is used for drug development at page 15. However, this is not what is claimed, nor is this described as

defining the "interactive clinical trial". Therefore, Iliadis fairly reads on an "interactive clinical trial" as Iliadis teaches computer simulations using pk and pd models.

Secondly, Merriam Webster (online at m-w.com/dictionary) defines "interactive" to mean: involving actions or inputs of a user, especially relating to two-way electronic communication (computer). Iliadis meet this definition of an "interactive" clinical trial by use of computer simulation models incorporating actions/inputs by users, as recited above. The rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

April 5, 2007
Lori A. Clow, Ph.D.
Art Unit 1631
Lori A. Clow
Patent Examiner